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10/755,720	01/12/2004	Peter Tontonoz	UCLA019.001A	1776
20995	7590	01/16/2008	EXAMINER	
KNOBBE MARTENS OLSON & BEAR LLP			BORIN, MICHAEL L	
2040 MAIN STREET			ART UNIT	PAPER NUMBER
FOURTEENTH FLOOR			1631	
IRVINE, CA 92614			NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/755,720	TONTONOZ ET AL.	
	Examiner Michael Borin	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on 25 October 2007.
- 2a) This action is FINAL. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-20 is/are pending in the application.
 - 4a) Of the above claim(s) 6-13 and 16-20 is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-5, 14 and 15 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>09/02/2004; 09/01/2006</u> | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of Claims

1. Claims 1-20 are pending.

Response to restriction requirement filed 10/25/2007 is acknowledged. Applicant elected, without traverse, Group I, claims 1-5,14,15. Claims 6-13, 16-20 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected groups.

As per election of species requirement set forth in the previous Office action, applicants have elected "treating" for claim 4.

Information Disclosure Statement

2. Applicants' Information Disclosure Statements filed 09/02/2004 and 09/01/2006 have been received and entered into the application. Accordingly, as reflected by the attached completed copies of forms PTO-1449, the cited references have been considered.

Claim Objections

3. Claim 14 is objected for the following informalities: Please correct the last word of the claim, "dependentt"

Claim Rejections - 35 USC § 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The claim lacks antecedent basis as the base claim 1 does not address "inflammatory disease" which is addressed in claim 15.

Claim Rejections - 35 USC § 112, first paragraph.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-5, 14, 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for particular oxysterol liver X receptor (LXR) agonists, does not reasonably provide enablement for any LXR agonist.

The claims are directed to method of reducing or treating inflammation in a mammal, comprising administering to the mammal a therapeutically effective amount of

an LXR agonist. In particular, the thrust of the invention is directed to such effect of LXR agonists on gene expression that, as per claim 2, said therapeutically effective amount of LXR agonist exhibits a relatively greater effect on expression of an inflammatory gene than on expression of a lipid metabolism gene, such that inflammation is reduced without a significant effect on lipid metabolism

Effect of LXR agonists on lipid metabolism is well known. See Song et al. (US 7078396) or by Elias et al (US 6184215), for example. Effect of LXR agonists on "inflammatory genes", and on inflammation in general is less certain. While some LXR agonists are shown to exert certain kinds of anti-inflammatory effect (see references used in art rejections below, and references cited in "Prior art of record" section), other agonist, to the contrary, show that they have pro-inflammatory effect. Thus, Liu et al. teach that oxysterols, i.e. LXR agonists, stimulate the secretion of IL-8 by macrophages, i.e., a proinflmmatory event (Liu et al, 1997; see Abstract).

The instant specification demonstrates effect of just two LXR agonists, GW3965 and TO9013117. The specification does not provide guidance on how to identify LXR agonists that would provide anti-inflammatory effect, and more specifically, would "exhibit a relatively greater effect on expression of an inflammatory gene than on expression of a lipid metabolism gene, such that inflammation is reduced without a significant effect on lipid metabolism".

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In view of the above, it is the Examiners position that with the insufficient guidance and working examples and in view of unpredictability and the state of art one skilled in the art could not make and/or use the invention with the claimed breadth without an undue amount of experimentation.

Claim Rejections - 35 USC § 102 and 103.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

6. There is a plurality of references either teaching or suggesting use of LXR agonists as anti-inflammatory agents. The references used in the following rejections

are exemplary. Non-exhaustive list of other relevant references is cited in "Prior art of record" section below.

7. Claims 1-5, 14 are rejected under 35 U.S.C. 102(e) as anticipated by Elias et al (US 6184215).

Elias et al. teach use of LXR agonists in treatment of such diseases as inflammation, such as cheilitis, chapped lips, nasal irritation and vulvovaginitis; psoriasis, dermatitis, etc. See col. 8.

In particular, with regard to claim 5, the reference address diseases, such as psoriasis, connective tissue diseases, which are also addressed in the reference (col. 8).

In particular, with regard to claim 14, the above cited disorders are macrophage dependent.

In particular, with regard to claim 2, the reference is silent about effect on either lipid metabolism genes or inflammatory genes. Yet the method steps, applying LXR agonist to treat or reduce inflammation, are the same. Under the principles of inherency, if a prior art method, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art. When the prior art method is the same as a method described in the specification, it can be assumed the method will inherently perform the claimed process. See MPEP 2112.02.

8. Claims 1,3-5,15 are rejected under 35 U.S.C. 102(e) as anticipated by Song et al. (US 7078396)

Song et al. teach use of agonists of liver X receptors for treating atherosclerosis.

See col. 1 and claim 1. Although the reference does not mention inflammation, per instant invention atherosclerosis is addressed as inflammatory disease – see instant claims 5, 15. Therefore, the reference is viewed as teaching the method as claimed.

9. Claims 1,3-5, 14,15 are rejected under 35 U.S.C. 102(e) as anticipated by Martin et al. (US 7115640).

Martin et al. teach use of agonists of liver X receptors for treating inflammation and plurality of other diseases. See claims 45, 54 and col. 55, in particular lines 14, 48.

In particular, with regard to claims 5,15, the reference teaches treatment of atherosclerosis.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

10. Claims 1-5, 14 are rejected under 35 U.S.C. 103(a) as obvious over Ohlsson et al (Clin. Invest. Vol 98, Number 1, 1996, 78-89) as evidenced by Elias et al (US 6184215).

Ohlsson et al teach that oxysterols inhibit binding of transcription factor AP-1 to DNA in macrophages, and thus reduces inflammatory response of macrophages. See Abstract, p. 87, second full paragraph. Although the reference does not teach reducing inflammation in a mammal, it would be obvious to an artisan that agents that reduce activation of macrophages will be of interest as anti-inflammatory agents because macrophage activation is an essential step of development of inflammatory response.

Unlike the instant claims, Ohlsson does not address the oxysterols as "LXR" agonists". However, it is well known that oxysterols are "LXR" agonists". See US 6184215, col. 2, bottom, for example.

Thus, the reference is viewed as suggesting anti-inflammatory effect of oxysterols, i.e., of "LXR" agonists"

Prior art made of record

11. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure: The references of Liu et al, 1998, (IDS, ref #25), Collins et al (2002, J. Med. Chem. 45, 1963-1966), Englund et al (2001, Atherosclerosis 158, 61-71) are cited to further show the state of the art teaching that LXR agonists have been shown to reduce inflammatory mediator production (e.g. nitric oxide (Liu), inflammatory

cytokines (Collins; Englund). Therefore, there is a clear rationale for using LXR ligands to evoke anti-inflammatory activity.

Conclusion.

12. No claims are allowed
13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Borin whose telephone number is (571) 272-0713. The examiner can normally be reached on 9am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Marjorie Moran can be reached on (571) 272-0720. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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mlb